BÖLÜM 16

NÖROİMMÜNOLOJİK HASTALIKLARDA KÖK HÜCRE TEDAVİSİ

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MULTİPLE SKLEROZ

Multipl skleroz (MS), merkezi sinir sisteminin kronik, inflamatuvar ve nörodejeneratif bir hastalığıdır.[1] Çoğunlukla 20 ila 50 yaşları arasındaki genç erişkin nüfusu etkiler. Olguların küçük bir kısmında ilk demiyelinizan klinik atak 18 yaşından önce olabilir ve bu durum pediatrik MS olarak tanımlanır.[2] Başlangıç MS'li hastaların %3-10'unda 16 yaşın altında, <%1'inde de 10 yaşın altındadır.[3] Pediatrik MS'in kendine has özellikleri vardır ve hastalık seyri erişkinlerden farklıdır. Çocukluk başlangıçlı MS hastalarının geri dönüşü olmayan engellilik durumlarına ulaşmaları daha uzun sürer ancak bunu erişkin başlangıçlı MS hastalarına göre daha genç yaşta yaparlar.[4]

Pediatrik başlangıçlı MS'in genel insidansı, 100.000 çocuk ve ergende 0.05 ila 2.85 arasında değişmektedir ve çalışmaların çoğu insidans oranlarını 100.000'de <1 olarak bildirmiştir.[5]

Hastalığın en yaygın formu, aralarda tam veya kısmi düzelmenin görüldüğü ataklarla seyreden "relapsing remitting (RR)" formudur. Primer progresif ve sekonder progresif MS oldukça nadirdir.[6] Çocuklarda en sık başvuru optik nörit, kranial sinir tutulumu belirtileri, beyin sapı tutulumu bulguları ve ataksidir.[4] İlk atak sırasında ADEM kliniği görülebilir ve polifokal bulgular ile seyredebilir.[7] Pediatrik MS tanısı klinik, görüntüleme ve laboratuvara dayanmaktadır. 2017 yılında revize edilen modifiye McDonald's kriterleri kullanılmaktadır. [8]

Atak tedavisinde, intravenöz metil prednizolon, tüm demiyelinizan hastalıklarda olduğu gibi birinci basamak tedavidir. Doz, tedavi süresi konusunda fikir birliği yoktur.[9] Steroide yanıt vermeyen hastalarda İVİG ve plazmaferez tedavi seçenekleri arasındadır.[10]

Pediatrik MS tanısı alan tüm hastalarda akut atak tedavisi sonrasında uzun süreli tedavi önerilmektedir. Uzun süreli tedavide interferon beta-1a ve 1b, glatiramer asetat ve teriflunamid gibi birinci basamak tedaviler ilk tercihtir.[11,12,13] Tedaviye tam yanıt alınamayan hastalarda natalizumab, fingolimod, siklofosfamid, rituksimab gibi ikinci basamak tedaviler kullanılır. Bu tedavilerin güvenliği, etkinliği ve tolere edilebilirliği ile ilgili veriler kısıtlıdır.[14,15] Tüm bu hastalık modifiye edici tedavilere rağmen MS'de nüks ve sekel oranları yüksektir.[16,17] Son yıllarda, hastalığın ilerlemesini durdurmak ve kalıcı nöral hasarı tersine çevirmeye yönelik, çeşitli kök hücre tedavileri gündeme

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için potansiyel bir hedef haline getirir.[109]

MOG antikorları ile ilişkili meydana gelen demiyelinizan hastalıklara, MOG antikoru ile ilişkili hastalık (MOGAD) adı verilir.[110] Edinilmiş demiyelinizan atak ile gelen çocukların üçte birinin MOG-Ab pozitif olduğu bildirilmiştir. MOG-antikorları, ADEM, transvers miyelit, izole optik nörit (ON) nöromiyelit optika spektrum bozuklukları (NMOSD) gibi tekrarlayan demiyelinizan hastalıklarda bulunabilir.[111]

MOGAD tanısı demiyelinizan bir atak (optik nörit, transvers miyelit,ADEM, serebral mono veya polifokal defisit, beyin sapı tutulumu veya serebellar defisit , sıklıkla nöbetle birlikte olan serebral kortikal ensefalit), anti-MOG antikor pozitifliği ve diğer demiyelinizan hastalıkların dışlanması ile konulur.[112]

MOGAD'ın akut atak tedavisi tüm demiyelinizan hastalıklarda olduğu gibi yüksek doz İV metilprednizolondur.[113]

MOGAD'da monofazik veya tekrarlayan klinik seyir görülebilmektedir. MOG antikorunun persiste etmesi durumunda tekrar etme ihtimalini arttırdığı görülmüştür.[114,115] MOGAD küçük çocuklarda ADEM ile kliniği ile monofazik bir seyir izlemesi muhtemel iken, daha büyük yaşlarda daha çok ON ve NMOSD fenotipi görülmekte olup bu çocuklarda relaps olma olasılığı daha yüksektir. [116]

MOGAD tedavisi için vaka serilerine ve uzman görüşüne dayanan kanıta dayalı kılavuzlar sınırlıdır.[117]

Tüm otoimmün hastalıklarda olduğu gibi hematopoetik kök hücre nakli agresif seyirli MOGAD için umut vaat etmektedir. Literatürde şuana kadar MOGAD'da kök hücre tedavisi yapılan tek vaka bulunmaktadır. Yirmi beş yaşında erkek hastanın ilk atağını 10 yaşında optik nörit olarak geçirdiği, tekrarlayan ataklar sonrası MS tanısı aldığı ve hastalık modifiye edici tedavilere başlandığı ancak klinik yanıt olmadığı bildirilmiştir. MOG antikoru tespit edilmesi üzerine azotiopürin ve alemtuzumab başlanan hastada klinik yanıt olmadığı için hastaya HKHN yapıldığı ve klinik yanıt alındığı bildirilmiştir.[118]

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